Prevalence of Aspirin Resistance in Stroke Patients in Phramongkutklao Hospital

Samart Nidhinandana MD*,
Siriprang Changchit MD **

** Department of Neurology and Psychiatry, Phramongkutklao Hospital, Bangkok, Thailand*
*** Neurologic Division,Department of Medicine, Phramongkutklao Hospital, Bangkok, Thailand*

Objective: *To study the prevalence of aspirin resistance in cerebrovascular disease patients in Phramongutklao hospital .*
Material and Method: *The acute ischemic and stable stroke patients who received aspirin at least 60 mg, at least 7 days and the last dose of aspirin at least 24 hours before blood test for platelet aggregation. ADP and Collagen were used as platelet aggregator.*
Results : *During July 2007- December 2008 , 141 cases of ischemic stroke were enrolled. "Aspirin resistant" was defined as mean aggregation more than 60% both ADP and Collagen. "Aspirin semi-responder" was mean aggregation less than 60% for ADP or Collagen.*
Conclusion: *Prevalence of aspirin resistance in Phramonkutklao hospital is 56 % (79/141), and there are relationship between aspirin resistance and timing in the first episode of stroke.*

Keywords: *Aspirin resistance, Ischemic stroke*

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Stroke is 3rd rank of mortality of male and 1st rank of mortality of female in Thailand[1]. For epidemiological data cerebrovascular disease consisted of ischemic stroke 70% and hemorrhagic stroke 30%[2]. Aspirin is an antithrombotic at a wide range of daily doses, from 30 -1,500 mg/day for prevention not only ischemic heart disease but also ischemic stroke. The mechanism of action of aspirin occurs to permanent inactivation of the cyclooxygenase (COX) activity of prostaglandin H (PGH) synthase I and II referred to COX1 and COX2 respectively. The effect of aspirin on inhibition platelet COX1 to prevent platelet aggregration and atherothrombosis.

The term"aspirin resistance" has been used to describe the inability of aspirin to produce a measurable response on ex vivo test of platelet function[3]. Incidence of aspirin resistance varies from 5-60%. The etiology of aspirin resistance is poorly understood depend on clinical, cellular mechanism and genetic factors. Many studies show aspirin resistance in coronary heart disease patients, in these patient groups have increased risk 3 times for recurrent ischemic heart disease. In one study show 27% aspirin resistance in Thailand[4,5]. Ischemic stroke patients with aspirin resistance increased risk of future cardiovascular events, including stroke, MI, or vascular death[6]. In 1999 ischemic stroke survivors in Phramongkutklao Hospital 452 case had recurrent stroke 31.39%, among these patients, 19% had aspirin for secondary prevention[7].

The objective of this study was to determine the prevalence of aspirin resistance in ischemic stroke patients in Phramongutklao Hospital.

Correspondence to:
Nidhinandana S, Department of Psychiatry and Neurology, Phramongkutkalo Hospital and College of Medicine, Bangkok 10400, Thailand.
Phone: 0-2354-7600
E-mail: msani@pmk.ac.th

Material and Method

The ischemic stroke survivors in neurological division, department of Medicine Phramongkutklao hospital were enrolled. Inclusion criteria; ischemic stroke patients age 18 years old or more whom attended in Neurologic division, Department of Medicine, Phramongkutklao Hospital whom were prescribed aspirin for secondary stroke prevention at least 60 mg daily for 7 days or more. Exclusion criteria; patient who were prescribe others antiplatelets such as ticlopidine,

dipyridamole, clopidogrel, NSAIDS, or aspirin compounds , heparin or low molecular weight heparin within 24 hours before collecting the blood. The patient underwent to operation within 1 week before collecting data ,The patient have a malignant paraproteinemias , hypercoagulable state or bleeding disorders, myeloproliferative disorders, chronic kidney disease, chronic liver disease.

The patients who met eligible criteria underwent blood sampling for platelet aggregation tests. In this study used platelet aggregometer, Adenosine diphosphate(ADP) and collagen as aggregator. Interpretation; the value of ADP and collagen will be presented by percentage in the vertical axis, normal people had an aggregation 60-90%. The patient who took aspirin should not aggregate but aspirin resistance will be aggregated[5,8-15]. Definition of aspirin resistance mean aggregation more than 60% both ADP or collagen.

Statistical analysis

For continuous data was shown in mean, standard error, and categorical data was described in percentage. Comparing categorical data among two groups by chi's square test or Fisher Exact test, For referring statistics T-test or non parametric test was test for 0.05 statistical significant.

Results

During July 2006-December 2007, 161 patients were enrolled, only141 patients were included to the analysis (20 patients were excluded because ineligible). 64% were male and 87% was first ever stroke. Most common risk factors of stroke were hypertension 83% and hyperlipidemia 59%. Among these, recurrent stroke was found 15.59%, however aspirin resistance was up to 56% (Table 1).

Recurrent ischemic stroke was occurred in average 48.87 days after first stroke (Table 2). After stroke onset until 30 days, we found that aspirin responsive cases were more than aspirin resistance group, however after 30 days, number of aspirin resistance was increased (Table 3).

Discussion

Prevalence of aspirin resistance was varies due to method of platelet aggregation test. However prevalence of poststroke survivors in Phramongkutklao Hospital was 56%. Dose of aspirin that have antiplatelet property was 50 mg/day[3]. The most population were chronic cases and this study we found that the relationship between first stroke and the onset of stroke were to the onset less than 30 days have an aspirin resistance 13 cases and aspirin responsiveness is 27 cases (p = 0.007). From the previous study in acute phase have low incidence however increasing with timing. We found no relation to it with time in repeated stroke patients. The data show no difference among aspirin dose 325 mg between resistance and responsiveness so we can conclude that the high dose

Table 1. Demographic data of Thai ischemic stroke patients (n = 141)

	Number	Percentage
sex Male	90	64
Female	51	36
First episode Stroke	122	87
Recurrent stroke	19	13
Smoking	58	41
hypertension	117	83
hyperlipidemia	83	59
Coronary heart disease	30	21
Vulvular heart disease	10	7
Atrial fibrillation	5	4
Recurrent stroke/first episode stroke	19/122	15.57
Dose of aspirin, mg (mean $\pm$ SE)	277.50 $\pm$ 22.50	120-300
Aspirin resistance	79	56

Table 2. Mean time after diagnosis of stroke and received aspirin treatment to the platelet aggregation test was done

	mean(days)	Standard error
First episode stroke	859.36	109.312
Recurrent stroke	48.87	31.1

Table 3. Relationship between aspirin resistance and duration after first episode of stroke

	Aspirin		P-value
	Response	Resistance	
< 30 days	27	13	0.007
31 days – 1 year	9	19	0.006
> 1 year	17	37	0.998
Total	53	69	0.921

*Pearson Chi square

of aspirin occur aspirin resistance less than low dose that why increase doses of aspirin was no significant antiplatelet effect.

Prior use of antiplatelet drugs, mainly aspirin, nearly halved the risk of early death among patients with ischemic stroke. And ischemic stroke may still occur in patients, it remains uncertain whether prophylactic use of aspirin reduces the severity of subsequent stroke[16].

The cause of high prevalence in this study was group of case are chronic CVD and we included aspirin semi responsiveness with other factors such as NSAIDS, other drugs, chance finding and lack of number of patient. However aspirin resistance was important problem to further study of prevalence in Thai population we had to collect proper data and need to randomized clinical trial for genuine prevalence of Thai aspirin resistance in ischemic stroke.

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ความชุกของภาวะดื้อต่อแอสไพรินในผู้ป่วยโรคหลอดเลือดสมองขาดเลือดในโรงพยาบาลพระมงกุฎเกล้า

สามารถ นิธินันทน์, สิริปราง จ่างจิน

วัตถุประสงค์: *เพื่อศึกษาความชุกของภาวะดื้อต่อแอสไพรินในผู้ป่วยโรคหลอดเลือดสมองขาดเลือดในโรงพยาบาลพระมงกุฎเกล้า*

วัสดุและวิธีการ: *ผู้ป่วยโรคหลอดเลือดสมองขาดเลือดทั้งเฉียบพลันและเรื้อรังทำการตรวจการทำงานของเกร็ดเลือดด้วยใช้ ADP และคอลลาเจนเป็นตัวกระตุ้นให้เกิดเกร็ดเลือดจับตัว*

ผลการศึกษา: *ระยะการศึกษาตั้งแต่เดือนกรกฎาคม 2550- ธันวาคม 2551 ได้รวบรวมผู้ป่วยโรคหลอดเลือดสมองตีบของแผนกประสาทวิทยา กองอายุรกรรม โรงพยาบาลพระมงกุฎเกล้าจำนวน 141 รายมาตรวจเลือดเพื่อหาการทำงานของเกร็ดเลือดโดยใช้ Adenosine diphosphate และคอลลาเจนเป็นตัวกระตุ้นให้เกร็ดเลือดจับตัว ภาวะดื้อต่อแอสไพรินหมายถึงเกร็ดเลือดมีการจับตัวมากกว่าร้อยละ 60 จากการใช้ ADPและคอลลาเจน และภาวะดื้อต่อแอสไพรินบางส่วนหมายถึงเกร็ดเลือดมีการจับตัวมากกว่าร้อยละ 60 จากการใช้ ADP หรือคอลลาเจนพบว่าความชุกของภาวะดื้อต่อแอสไพรินร้อยละ 56*

สรุป: *ความชุกของภาวะดื้อต่อแอสไพรินในผู้ป่วยโรคหลอดเลือดสมองตีบในโรงพยาบาลพระมงกุฎเกล้าพบร้อยละ 56*